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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,238	03/29/2004	Kishore K. Wary	D6563	3362

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
10/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/812,238	WARY ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,14,15 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-9, 14-15 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 8/9/07, is acknowledged.

2. Claims 8-9, 14-15 and 32 are pending and under examination in the instant application as they read on a method of inhibiting cell-cell interaction, a method of treating a patient having a pathological condition and a method of inhibiting angiogenesis and the formation of capillaries in patient with antibody directed against a peptide comprises CRGDD sequence, angiogenesis, inflammation and tumor growth as the species.

3. In view of the amendment filed on 8/9/07, only the following rejections are remained.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 8-9 and 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Vassilev et al (Blood. 1999 Jun 1;93(11):3624-31), as is evidenced by Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) for the same reasons set forth in the previous Office Actions mailed 9/30/05, 5/31/06 and 3/9/07.

Applicant's arguments, filed 8/9/07, have been fully considered, but have not been found convincing.

Applicant submits that the instant invention teaches a specific antibody directed against a peptide consisting of SEQ ID No. 41 or consisting of SEQ ID No. 2 that is derived from a cell surface vascular endothelial growth factor and type I collagen inducible protein (VCIP) consisting of SEQ ID No. 13. The antibody taught by the instant invention is able to block binding of $\alpha v\beta 3$ and/or $\alpha 5\beta 1$ integrins to the cell surface vascular endothelial growth factor and type I collagen inducible protein (VCIP), thereby inhibiting the cell-cell interaction. Applicant submits that Vassilev et al teach a pool of antibodies that are able to bind to a RGD-motif containing protein. However, Vassilev et al do not identify one antibody in particular that is able to mediate binding to the RGD-motif containing proteins. Further, Vasilev et al demonstrate that their pool of antibodies can bind to fibronectin, fibrinogen, vitronectin, VWF and laminin in a dose-dependent manner but do not show or demonstrate that it can bind to VCIP. Furthermore, the proteins taught by Vassilev et al are all basement membrane proteins. It is known in the art that there are many adhesive proteins present in extracellular matrices and in the blood that contain the tripeptide arginine-glycine-aspartic acid (RGD) as their cell recognition site. The RGD sequences of each of the adhesive proteins are recognized by at least one member of a family of structurally related receptors, integrins. Some of these receptors bind to the RGD sequence of a

single adhesion protein only, whereas others recognize groups of them. Thus, the conformation of the RGD sequence in the individual proteins is critical to this recognition specificity. Hence, one of skill in the art cannot assume that the unidentified antibodies in the pool taught by Vassilev et al would also bind the VCIP protein identified by the instant invention.

The Examiner agrees with applicant to the extent that the structural scaffold of RGD containing protein is important in a functionally optimal conformation. However, the Examiner disagrees with applicant that one of skill in the art cannot assume that referenced anti-RGD antibody taught by Vassilev et al would bind the VCIP protein. The referenced antibody recognizes and binds a motif that is present in several RGD containing proteins and peptides. Accordingly, the anti-RGD antibodies taught by Vassilev et al would bind the claimed SEQ ID Nos: 41, 2, and 13 because they contain the RGD-motif, wherein said antibody would function as the claimed antibodies, irrespective of the conformation of the RGD sequence in the individual proteins. Because VCIP possess RGD binding motif similar to those found in native ligands, such as fibronectin, fibrinogen, vitronectin, VWF and laminin, the anti-RGD antibody taught by Vassilev et al inherently binds to the claimed VCIP protein. The shared scaffold is used for the stereochemical presentation of the RGD site for receptor recognition, which makes the RGD epitope accessible to the antibody.

Applicant submits that the instantly claimed methods use a specific antibody directed to "specific peptides", derived from VCIP. It is not inherent based on the teachings of Vassilev et al, cited by the Examiner, that the unidentified antibodies, that bind RGD-motif containing basement membrane proteins, would also bind the RGD-motif containing VCIP expressed by endothelial cells, given that the conformation of the RGD would be different in VCIP versus the proteins taught by Vassilev et al. At a minimum, neither of the references cited by the Examiner teach the antibodies against peptide of SEQ ID NO: 2 or 41 derived from the protein represented by SEQ ID NO: 13.

Contrary to Applicant assertion, the anti-RGD antibody taught by Vassilev et al would bind to the claimed VCIP of SEQ ID NO: 13 and the peptides SEQ ID NOS: 2 and 41 because they all possess the RGD epitope which the anti-RGD antibody recognizes irrespective of the structural conformational of the RGD. VCIP possess RGD binding motif similar to those found in native ligands, such as fibronectin, fibrinogen, vitronectin, VWF and laminin, the anti-RGD antibody taught by Vassilev et al inherently binds to the claimed VCIP protein.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 15 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,807,819 in view of U.S. Pat. No. 5,567,440 and Vassilev et al as is evidenced by Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) for the same reasons set forth in the previous Office Action mailed 3/9/07.

Applicant's arguments, filed 8/9/07, have been fully considered, but have not been found convincing.

Applicant submits that the instant invention teaches a specific antibody directed against a peptide of SEQ ID No. 41 or SEQ ID No. 2 that is derived from VCIP consisting of SEQ ID NO: 13. This antibody blocks the binding of $\alpha v\beta 3$ and/or $\alpha 5\beta 1$ integrins to the cell surface vascular endothelial growth factor and type I collagen inducible protein (VCIP), thereby inhibiting the cell-cell interaction. Vassilev et al teach a pool of antibodies that are able to bind RGD-containing protein and to basement proteins such as fibronectin, vitronectin, VWF and laminin in a dose dependent manner. There is no teaching or suggestion in this reference that the antibody would also bind peptide/protein with SEQ ID No: 2, 13 and 41 as taught by the instant invention. Applicant submits that it is known that the extracellular matrices and blood comprise many adhesive proteins that contain RGD as their recognition site. Applicant submits that some of the structurally related receptors such as integrins bind to the RGD sequence of a single adhesion protein whereas others recognize groups of them. Thus, the ability of the receptor to recognize the RGD sequence in the individuals critically depends on the conformation of the RGD sequence in the individual proteins. This teaching along with the absence of demonstration by Vassilev et al of their antibodies bind to the instant peptides, Applicant contends that one skilled in the art cannot expect success in merely substituting the antibody of Vassilev et al in the instantly claimed method.

However, Applicant's argument attempts to limit the antibody bind peptide/protein with SEQ ID NO: 2, 13 and 41 in a manner inconsistent with the well-known and art-recognized specificity of antibody interaction with epitopes defined by particular amino acid sequences. That is an antibody "cross-reacts", i.e., binds to more than one protein sequence. It means that the antibody does bind more than one protein based on shared amino acid sequence. Claimed SEQ ID NOS: 2, 13, and 41 share RGD motif with other proteins such as fibronectin, fibrinogen, vitronectin, VWF and laminin, the anti-RGD antibody taught by Vassilev et al inherently binds to the claimed VCIP protein, irrespective of the structural conformation of the RGD. This shared scaffold is used for the stereochemical presentation of the RGD site for receptor recognition, which makes the RGD epitope accessible to the antibody.

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 2, 2007

Maher Haddad

Maher Haddad, Ph.D.
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